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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,286	NUNOMURA, KIYOTADA	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *105,106,108-110 and 116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105,106,108-110 and 116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *02092003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to an amendment filed on September 2, 2003. Claims 105, 106, 108-110 and 116 were previously pending. Applicant amended claim 105. Claims 105, 106, 108-110 and 116 are pending and will be examined.

2. Applicant's amendment overcame the rejection of claims 105, 106, 108-110 and 116 under 35 U.S.C. 103(a) over van Gemen et al. The other rejections are maintained for reasons given in the "Response to Arguments" section".

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on September 2, 2003 was filed after the mailing date of the non-final office action on May 6, 2003. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

4. Applicant's arguments filed September 2, 2003 have been fully considered but they are not persuasive. Regarding rejection of claims 105, 106 and 116 under 35 U.S.C. 102(e) over Aoyagi et al., Applicants argue that the reference does not provide all of the limitations of claim 105, since it does not disclose a system indicating a positive result when the amount of analyte polynucleotide is greater than a predetermined value, and a negative result when the amount of analyte polynucleotide is less than a predetermined value, since values of Ct greater than 40 indicate no samples and values of Ct below 40 indicate presence of the sample.

However, Ct is an indicator of the presence or absence of the polynucleotide in the sample. Therefore, value of Ct greater than 40 is a negative result , indicating that the amount of polynucleotide present is below a threshold level, and a value of Ct less than 40 is a positive result,

indicating that the amount of polynucleotide present is below a threshold level. The rejection is maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Before proceeding with the rejection, Applicants' definition of a "pseudo target" is provided (page 8, lines 8-14):

"A "pseudo target" is a polynucleotide that can be co-amplified with the analyte polynucleotide in a single amplification reaction. The pseudo target and the analyte polynucleotide may be amplified using the same set of oligonucleotide primers. However, it is also possible for the pseudo target and the analyte polynucleotide to co-amplify using independent primer sets. The pseudo target and the analyte polynucleotide will be nonidentical molecules so that the analyte polynucleotide and the pseudo target can be distinguished from each other."

Therefore, a pseudo target according to this definition can be any polynucleotide which is co-amplified with the target polynucleotide.

7. Claims 105, 106, 108 and 116 are rejected under 35 U.S.C. 102(e) as being anticipated by Aoyagi et al. (U. S. Patent No. 5,952,202; cited in the previous office action).

Regarding claims 105 and 106, Aoyagi et al. real-time detection of nucleic acids by co-amplification of the target polynucleotide with an internal control polynucleotide (ICP). The target and internal control polynucleotides are amplified with their respective primers. The amplification

products are detected with probes specific for the target and internal control, respectively (col. 7, lines 16-35). The probes are self-quenching fluorescence probes, which have a reporter dye and quencher dye attached to the opposite ends of the probes. During the polymerization reaction the polymerase digests the probes to separate the reporter dye from the quencher dye, and the increased fluorescence indicates the presence of amplified products (col. 8, lines 10-41; Fig. 1; col. 14, lines 45-63).

The signal is detected as a Ct value, which indicates the presence of a fluorescence signal distinguishable from the background, indicating presence of a target polynucleotide in the sample (col. 18, lines 45-61). Aoyagi et al. teach detection of *Mycoplasma* DNA by a process comprising co-amplification of *Mycoplasma* cDNA and an internal control polynucleotide using *Mycoplasma*-specific probe labeled with FAM (target) and JOE (control). The pre-determined threshold Ct value of 40 (negative result) indicates that there is no detectable DNA in the sample, whereas Ct values below 40 (positive result) indicate presence of the target and control polynucleoties (col. 21, lines 25-36; col. 22, lines 1-26; Fig. 9).

Regarding claim 108, Aoyagi et al. teach reporters which can be either fluorescent or chemiluminescent (col. 4, lines 54-57).

Regarding claim 116, Aoyagi et al. teach detection of the signal using a fluorescence detection system comprising a lens, a fiber optic and a CCD camera (col. 17, lines 63-67; col. 18, lines 1-42).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 109 and 110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. as applied to claim 105 above, and further in view of Jurriaans et al. (Immunol. Letters, vol. 51, pp. 15-22, 1996; cited in the previous office action).

A) Claim 109 is drawn to analyte polynucleotide being a viral polynucleotide, and claim 110 is drawn to the viral polynucleotide being an HIV-1, HIV-2, HBV or HCV polynucleotide.

B) Teachings of Aoyagi et al. are described above. Regarding claims 109 and 110 Aoyagi et al. teaches application of the methods to target-specific assays for pathogen detection, which can be performed in a multiplex format (col. 11, lines 30-47). Aoyagi et al. do not explicitly teach detection of HIV-1, HIV-2, HBV or HCV.

C) Jurriaans et al. teach determination of the amounts of HIV-1 RNA and DNA in clinical samples by amplification methods including NASBA and PCR. It was found that the levels of viral RNA and DNA measured over a period of time can serve as indicators of whether and how fast the disease will develop (Fig. 2, 3; pages 18-21). In particular, the levels of single-LTR DNA may be valuable in detecting early signals of the spread of the infection (page 20, the last paragraph, continued on page 21). In addition, monitoring of single-LTR DNA enables accurate monitoring of e response to antiviral therapy (page 21, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the method of Aoyagi et al. for the detection of HIV-1 DNA of Jurriaans et al. The motivation to do so, provided by Aoyagi et al., would have been that using real-time amplification with internal controls provide a rapid and accurate nucleic acid amplification assay (Abstract). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of

the invention to have detected HIV-1 of Jurriaans et al. in the method of Aoyagi et al. The motivation to do so, provided by of Jurriaans et al., would have been that accurate detection of HIV-1 levels in serum would allow prognosis of HIV progression and treatment (page 20, last paragraph; page 21).

10. No claims are allowed.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

The examiner will move to the new office in Alexandria on January 8, 2004. The new phone number in that office is (571) 272-0789. Gary Benzion will move to the new office on January 22, 2004. His new phone number is (571) 272-0782.

TS
December 20, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER